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Intracranial Pressure Sensor

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UNDER MY SUPERVISION BY

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ENTITLED

INTRACRANIAL PRESSURE SENSOR

BE ACCEPTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
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INTRACRANIAL PRESSURE SENSOR

By

Matthew Murray, Jared Shimada
Equal Participants

SENIOR DESIGN PROJECT REPORT

Submitted to
the Department of Bioengineering

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Abstract

Idiopathic Intracranial Hypertension (IIH) also known as Pseudotumor Cerebri is a condition resulting from an increase of Cerebrospinal Fluid (CSF), a fluid that helps to protect the brain and spinal cord, in the cranial cavity. Currently the only treatment method for this health condition is the draining of the fluid via implanted intracranial shunts that get clogged in approximately 50% of patients. Clogged shunts can only be detected when IIH symptoms begin to reappear. We propose to create an ultrasound-read intracranial pressure sensor used to supplement shunts implanted in patients who suffer from Idiopathic Intracranial Hypertension. This will provide immediate knowledge of clogged catheters, preventing further damage to accrue due to an unknown buildup of pressure, prior to, and when symptoms begin to show. This pressure sensor will significantly benefit the current treatment method by allowing easy and immediate diagnosis of the current condition of the CSF and the shunt. This completely mitigates harmful symptoms that occur while Idiopathic Intracranial hypertension is left untreated and provides a simple method of keeping track of the patient's current state, enabling doctors to know immediately when an additional shunt is necessary. In this paper, we design and fabricate an intracranial pressure sensor that is intended to be read via ultrasound. Our experiments show that our design is capable of reading pressure changes in water. Using a light microscope, we were also able to correlate the movement of the air-liquid interface in the sensor channel to pressure changes. From these findings, we hope that the sensitivity of the sensor can be further refined and will be tested for visibility under ultrasound.

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Chapter 1 - Introduction

1.1 Background

Idiopathic Intracranial Hypertension, also known as Pseudotumor- Cerebri, is a chronic neurological disorder that presents symptoms similar to those created by a brain tumor. This disorder generates increased intracranial pressure in the absence of a tumor, infection, or hypertensive encephalopathy. Some symptoms associated with this condition are headaches, nausea, Pulsatile Tinnitus, horizontal double vision, temporary obstructions to vision such as dimming of vision and complete blackout of vision, and loss of color vision. The specific cause of Idiopathic Intracranial Hypertension is unknown; however, this condition is attributed to the body's inability to reabsorb CSF, a fluid that naturally helps to protect the brain and spinal cord. Some of the other health problems associated with Idiopathic Intracranial Hypertension include various head injuries, Lupus, measles, malnutrition, and anemia. Additionally, certain medicines such as oral contraceptives, steroids, Sulfa based medicines, and some chemotherapeutic drugs.

Figure 1-1: Comparison between Normal CSF Flow and a build of CSF in the cranial cavity ("About Your Ventriculoperitoneal (VP) Shunt Surgery").

The practice for treating Idiopathic Intracranial Hypertension involves shunting, the use of polymer-based tubes to drain the excess fluid from the cerebrum. This process utilizes two catheters and a valve to redirect CSF from the cranial cavity to the peritoneal cavity. When the fluid reaches the peritoneal cavity, it is reabsorbed into the body. Shunting allows for the treatment of Idiopathic Intracranial Hypertension without causing hypotension or abnormally low pressure in the brain.

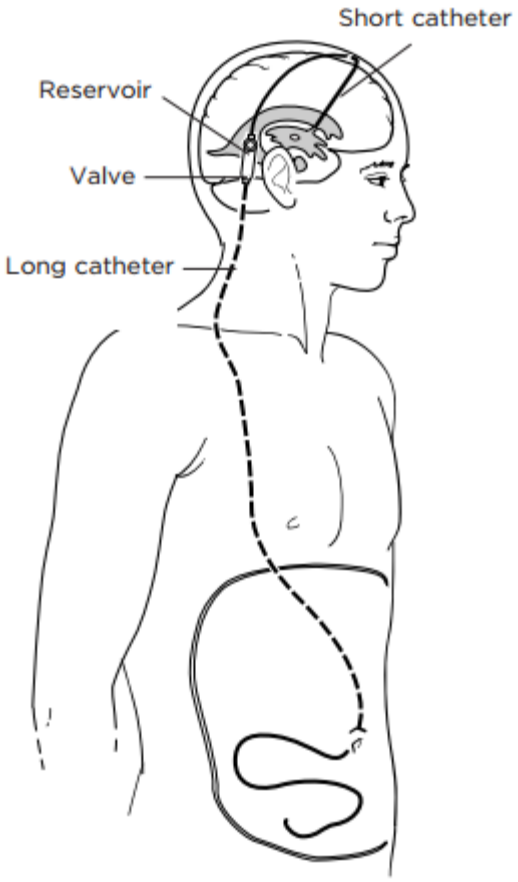


Figure 1-2: Diagram of CSF Flow through an implanted shunt ("About Your Ventriculoperitoneal (VP) Shunt Surgery").

Shunting appears to be a promising solution to this condition; however, there are many obstacles. The most significant of these is the clogging of shunts. Shunt clogging occurs in approximately 50% of all cases and can occur multiple times. When the shunt becomes partially or completely clogged, the flow of CSF into the peritoneal cavity becomes compromised. This reduction or cease of this flow will cause intracranial pressure to

increase. To correct this problem, another shunt can be implanted to replace the clogged one; however, the clogged shunt cannot be removed due to the high risks associated with the procedure. If repeated shunt clogging occurs with a single patient, this person will be left with many nonfunctioning shunts implanted in their head.

1.2 Review of Literature

1.2.1 Intracranial Pressure

When the pressure in a patient's brain becomes too high, a system is implemented into their head that regulates their intracranial pressure. This system both measures, and adjusts the pressure in their brain. A shunt system drains extra fluid, through a valve attached to a pressure sensor. If the pressure is above the threshold value then the valve remains open, allowing the cerebral fluid to drain. If the pressure begins to drop, the valve closes. The device is readable through a handheld “reader.” This “reader” sends magnetic radio waves to supply the sensors in the shunt with power, and measure temperature and pressure and relay them to the device (Görtz).

The system currently used to document health records is very text-heavy and inefficient. The use of photographic records would greatly supplement the current documentation. This method, however, is hindered by the current equipment required to obtain photographic records. This equipment requires trained technicians to operate expensive, tabletop units. With the evolution of smartphones, a 3D printable attachment to smartphone cameras that enable high quality photos of the eye, generating proper resolution and lighting was proposed. This method has successfully photo documented both normal and abnormal retinal findings (Myung).

There are several diseases that are linked to changes in intracranial pressure. Some of these include Intracranial Hypertension, Intracranial Hypotension, and meningitis. This generates a need for a chronic implantable device. At the minimum, this device consists of a pressure-sensing element with a mode of transmitting the data to an external unit. Issues that appear when designing this system include biocompatibility, host response, surgical placement, and

the comfort of the patient. A general design was created that addresses interactions between the system and the body, and efficient telemetry (Yu).

1.2.2 Intraocular Pressure

In addition to intracranial pressure, we believed that also doing a literature review on intraocular pressure would benefit our project. Although some of these articles do not directly correlate to the production of an intracranial pressure sensor, the information found does help to gain a better understanding of downscaling sensors for use in smaller areas of the body. Moreover, the testing procedure for biocompatibility aids in the development of listing all possible materials that could possibly be utilized in detecting intracranial pressure.

Intraocular pressure is a relatively consistent way for diagnosing glaucoma, a disease that causes damage to the eye's optic nerve. Single time measurements may miss peaks in intraocular pressure that may only occur at night. A chip-less contact lens, composed of a thin film capacitor and a sensing coil designed to detect deformation in the corneal curvature is the proposed method for monitoring intraocular pressure throughout the day and night (Chen).

The conventional contact lens is used by many people for the sole use of vision correction. Possible methods to integrate micro-devices into contact lenses were discussed. A couple of the devices or features talked about include a semi-transparent display on the surface of the lens and use of small biosensors on the surface of the eye. Additionally, the paper discusses methods to make such a device biocompatible in rabbits (Ho).

Measuring intraocular pressure has a variety of physiologic parameters that depend on the circadian variations with unpredictable fluctuations. Current methods of measuring intraocular pressure include diurnal or 24-hour intraocular pressure measurements which are both inconvenient and expensive. The goal of continuous intraocular pressure monitoring is

to provide 24-hour measurements through either a contact lens-based pressure sensor, or an implantable pressure sensor (Sit).

Goldmann applanation tonometry (GAT) has been the standard for tonometry, the procedure to determine intraocular pressure, for over 50 years. GAT has many limitations. Dynamic Contour tonometry is cornea-independent but requires great technical skill. Rebound tonometry doesn't require anesthetics. The ocular response analyzer can provide readings relevant to glaucoma risks. There is no perfect method for tonometry and clinicians must weigh the pros and cons when deciding which method to use (Okafor).

A contact lens consisting of the tear film is used to provide continuous surveillance of the health conditions in a patient in a minimally invasive manner. These sensors have a response time of approximately 35 seconds, and are built to function at temperatures found on the surface of the eye. Their output is stable for up to 24 hours. A polymer substrate is used and molded into the shape of a contact lens to provide the monitoring of L-lactate levels in tear fluid (Thomas).

A wireless, microfluidic pressure sensor composed of Polydimethylsiloxane (PDMS) and glycerol has been created for point-of-care glaucoma diagnosis. The IOP is measured using Laplace's principle where the pressure inside the chamber is determined by loading pressure, and measured by the microfluidic pressure sensor located inside. PDMS is used due to its flexible, polymeric membrane. Its surface is also has excellent elasticity and flexibility with a Young's modulus of 500kPa (Yan).

1.3 Statement of Project Objectives

1.3.1 Problem Statement

We propose to create an intracranial pressure sensor used to supplement shunts. This will be read through ultrasound to detect the current pressure in the cranial cavity and will provide immediate knowledge of clogged catheters, preventing further damage to accrue due to an unknown buildup of pressure, prior to, and when symptoms begin to show. Our device will be composed of two primary sections, the catheters that drain fluid from the cranial cavity into the peritoneal cavity, and the pressure sensor itself.

The pressure sensor will consist of a channel that leads to a reservoir filled with air. The fluid enters the cavity and the position of the fluid/air line in the channel determines the current pressure within the cranial cavity. Normally the pressure will remain constant if the catheters are working properly, but in the event that the catheters become clogged, this will provide an early indication of the clogging. The pressure sensor itself will be made of epoxy created from a 3D printed mold. It will be bonded to a thin epoxy base to ensure sterility and to prevent leakage. The epoxy base is then bonded to a glass base. The mouth of the channel has a tapered end, over which the catheter is attached and sealed. The catheter itself will be gas permeable with a diameter of approximately 50-100 microns. This device will not prevent clogging within catheters but it will significantly improve our ability to detect clogged catheters and implement a new catheter before the pressure in the cranial cavity rises significantly and causes either temporary or permanent damage to the patient.

Our proposed budget amounted to $1400. This was composed by 4-5 3D Prints at $500, .5 Gallons of PDMS at $300, $200 for various plastics and substrates, and $100 for miscellaneous items. Our grant proposal netted us $1000 dollars to work on this project. We are making modifications to our overall budget by improving our SolidWorks designs to require fewer 3D Prints. We have been working with Dr. Emre Araci as well as partially with another senior design group working on an intraocular pressure sensor.

1.3.2 Objectives

Aside from our primary objective of creating an ultrasound read intracranial pressure sensor, we wanted to focus on two key aspects of the sensor: sensitivity and specificity. Increased sensitivity of our sensor would allow physicians to detect even the slightest changes in patients' intracranial pressure. Detecting a minute increase in pressure could potentially provide earlier detection of clogged shunts, thus allowing physicians to treat the condition sooner. To reach this goal, we will test different channel sizes used in the sensor and observe which size provides us with the optimal sensitivity. In terms of specificity, we want to be able to accurately correlate movement of the air-liquid interface to a quantitative pressure change. To accomplish this, we hope to test the device at different pressures, pinpoint where the air-liquid interface is located in our sensor at specific pressures, and to quantify the distance the interface travelled per unit of pressure.

In addition to the goals and objectives previously discussed, we hope to learn more about the fabrication and theory of microfluidic devices, obtain contacts and experience with our partner facilities, and to enjoy the experience of designing, fabricating, and testing our own device.

Chapter 2 – Systems Overview

2.1 Benchmark Results

There are currently three other ways to monitor intracranial pressure. These methods consist of an Intraventricular Catheter, a Subdural Screw, and an Epidural Sensor. The first, the Intraventricular Catheter is the most accurate method and employs the use of a catheter that is inserted into the brain into the lateral ventricle. This method enables the draining of Cerebrospinal Fluid. The Subdural Screw is a method used for instantaneous pressure measurement. A hollow screw is placed through the dura mater, the membrane that protects the spinal cord and brain. Lastly the Epidural Sensor allows for a minimally invasive reading of the pressure inside the brain. It consists of a sensor that is placed between the skull and the external tissue. This method does not include the draining of Cerebrospinal Fluid. Our device will be similar to a combination of the Intraventricular Catheter and the Epidural Sensor, connecting an Epidural sensor to a catheter to enable accurate reading of Intracranial Pressure while providing drainage of Cerebrospinal Fluid (Kantor).

2.2 Customer Needs

After researching current methods of detecting intracranial pressure, we have determined that our device will have to be affordable, minimally invasive, user-friendly, highly specific, and highly sensitive as well as provide rapid results. While current methods employ one or some of these characteristics, none of them employ all of them. Our

design for an intracranial pressure sensor was created with these characteristics and features in mind.

2.3 Team Project and Management

2.3.1 Team Management

Our team consisted of two members, Matthew Murray and Jared Shimada. After much discussion, we concluded that assigning specific responsibilities to each member would not benefit the progress of the team since the facilities we would be using for fabrication and testing enforced a buddy-system policy. There would not be a point in time during this project where each of us would be able to work on different components without violating facility policies. As a result, our team ultimately made the decision to be equally responsible for all aspects of the project including but not limited to literature research, fabrication, design, experimental testing, documentation, and miscellaneous logistics.

In order to maintain regular communication between our advisor and the team and to receive constructive feedback on our project, we scheduled weekly meetings at the end of every week with Dr. Araci and presented our progress to colleagues and peers approximately every two to three weeks.

2.3.2 Design Process

Our design process began with a pencil and paper drawing of our sensor. We created a SolidWorks design but quickly converted this to AutoCAD once we realized we would be able to generate more sensors per mold while minimizing the cost. From our AutoCAD model we created masks via Soft-Lithography. These masks served to create our molds out of PDMS, which we then poured epoxy into to create our sensor halves. When creating the top mold out of PDMS we partially cured the mask before

adding more PDMS to the reservoir to increase its size. We plasma treated the sensor halves and bonded them together under UV light. With our sensors completed, we inserted 50 micron diameter capillary tubes into the channels to enable testing within variable pressure conditions.

2.3.3 Budget

Approaching our project we realized we would need to purchase PDMS, Capillary tubes, and Epoxy, as well as pay for services including the processing of our masks for Soft-Lithography and various miscellaneous chemicals used in the general procedures associated with our design process. We were able to receive a grant from the Santa Clara University School of Engineering Undergraduate Programs for $1000 dollars. The primary uses for this grant were to purchase a half gallon of PDMS at the price of $300 dollars, to pay for the screening and production of the masks from our AutoCAD design at the cost of $200 dollars. To obtain the capillary tubes for producing testable models of our device at the cost of $200 dollars, and to order Epoxy, TP5, cross linker, and other miscellaneous chemicals costing around $300 dollars.

2.3.4 Timeline

We were delayed in the fall due to the construction of the microfluidics lab. During this time, we used our time to conduct a literature review on intracranial and intraocular pressure and to start a preliminary concept for our sensor. By the end of January 2016, we created and sent out our AutoCAD molds by early February, receiving our masks three days later. This enabled us to begin creating our sensors, with each step of the first prototype taking approximately a week to accomplish. By March 4th we had our first complete prototype, using Epoxy 61 and proceeded to begin running tests under water to determine functionality of the sensor. Once functionality was determined we looked into a softer, higher viscosity epoxy, Epoxy 68 to both create sensors that could obtain greater resolution under visible light and Ultrasound while streamlining the process of creating the sensor halves. By early May we had successfully quantified the pressure changes represented by the sensors

and we hoped to proceed with testing via Ultrasound Machine before the end of May; however, we were unable to do so.

2.3.5 Challenges and Constraints

The primary risks associated with our project were related to quality specifications, sterility, and material compatibility. It was critical to ensure the dimensions we received on our masks matched the exact 100, 200, and 300 micron specifications. Next we considered the quality of the PDMS in our molds. First we would aerate our masks with TP5 to ensure a clean surface for our molds to form. When producing our molds we would incubate them for a sufficient time to allow the material to sufficiently cure before vacuum treating the molds to remove any excess air bubbles. The next issue arose with creating the sensor halves from epoxy. Epoxy does not like to adhere to PDMS, and will constantly recede to the center of the mold, away from the tapered end. To combat this we used a softer, high viscosity Epoxy as well as a UV gun that enabled instantaneous curing of the Epoxy in the taper. When implementing the capillary tubes into the sensors we had to be careful not to seal the inside of the tubes while bonding them to the sensor. Throughout this entire process, complete sterility was maintained within our Microfluidics lab.

Chapter 3 – Design, Fabrication, Testing, and Results

3.1 Experimental Protocol

3.1.1 Design

We began by creating a sketch of the design concept based upon our customer needs and specifications. Our initial design concept was made with the theory behind the device in mind instead of aesthetics. Once we had the basic working concepts of the device on paper, we moved on to making the device with aesthetics in mind.

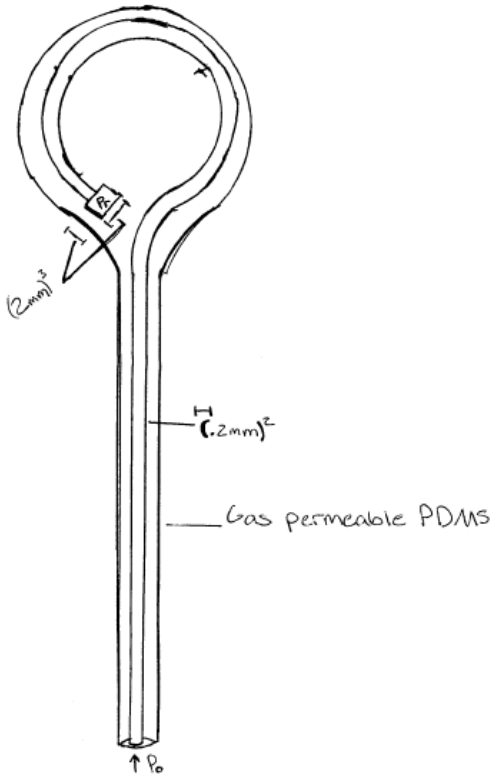


Figure 3-1: Design Schematic/Preliminary Sketch

The next generation of our design was created in SolidWorks. We wanted to use SolidWorks to create a negative mold of our device, thus allowing us to create multiple devices from the same reusable mold by pouring epoxy directly into it. From here, the plan was to utilize the 3-D Printer at Santa Clara University's Frugal Innovation Laboratory to produce these molds. However, our advisor mentioned to us the extra cost of materials as well as the extra time it would take the 3-D printer to make our molds. In addition to this, specificity was a concern because we were not sure if the 3-D printer was capable of making 100, 200, and 300 micron diameter channels accurately.

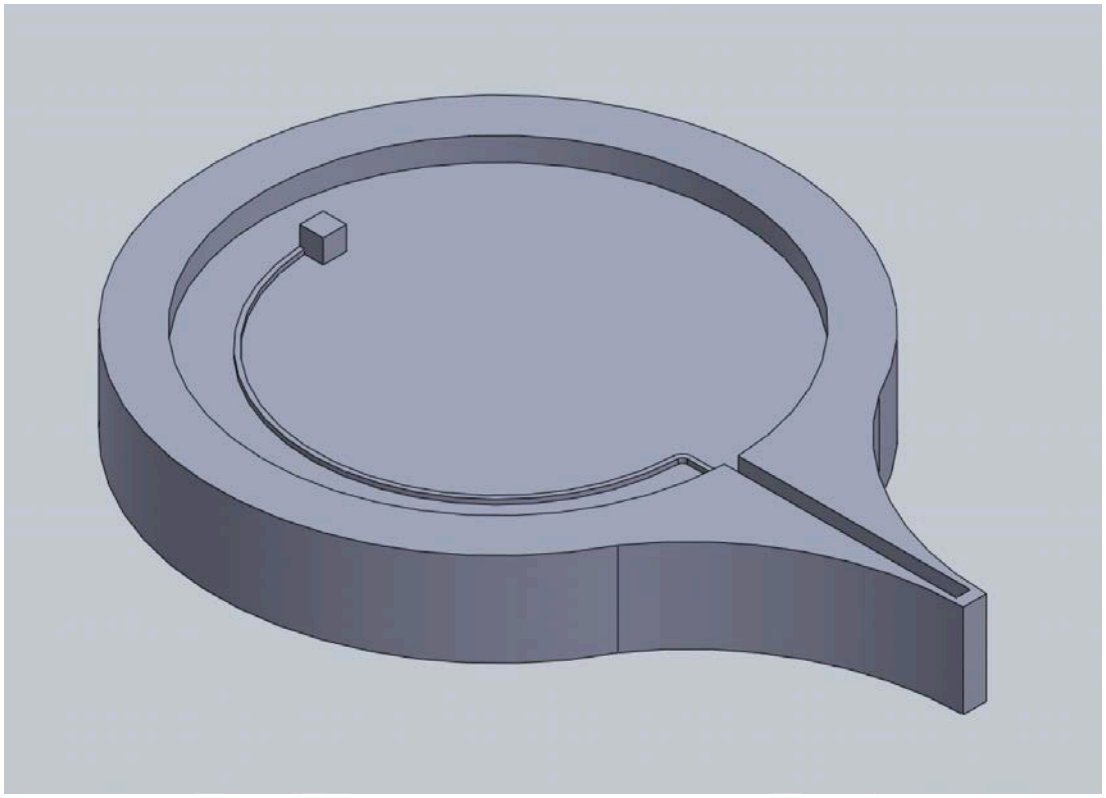


Figure 3-2: SolidWorks Design of Second Generation Intracranial Pressure Sensor. This image shows the negative of the sensor.

Our advisor then recommended that we attempt to produce our devices via Soft-Lithography, a technique used to replicate structures using photomasks (See Soft-Lithography section in Fabrication). This method of device fabrication would require us to make new molds every time we wanted to produce new samples; however, we could reuse the mask used to create our molds and we would be able to produce

multiple samples on the same mold, thus reducing the number of molds created. As a result, we converted our SolidWorks design to AutoCAD and made changes to the design. In this third generation of our design concept, we increased the size of the gas reservoir to allow for higher sensitivity and specificity and created a tapered end on the sensor to allow for attachment of a capillary tube. For this design, we created three different sensor templates, each with different channel diameters (100, 200, 300 micron diameter channels). After designing each template for the molds, we created a template for our mask. On a 4 inch diameter template for the mask, we were able to fit nine sensor templates (three of each different template).

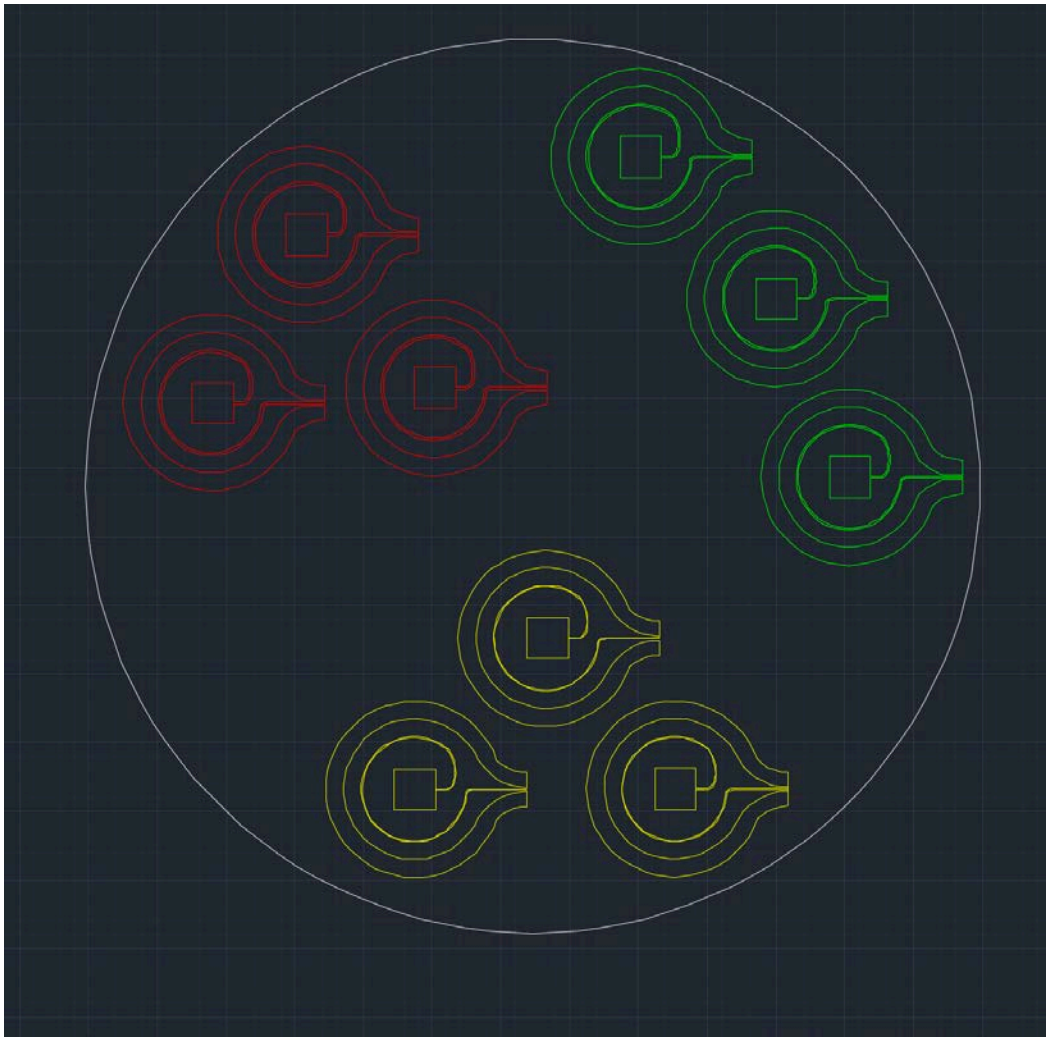


Figure 3-3: AutoCAD design of 100 (yellow), 200(green), and 300 (red) micron channel diameter sensors.

3.1.2 Fabrication

The Soft-Lithography process begins with a silicon wafer. Photoresist is applied to the silicon wafer, after which the mask is added. The mask is exposed to ultraviolet light and then the photoresist is dissolved. The mask is now contains a negative of the structure which is required to create the PDMS molds.

Once the photomasks were completed, we moved onto creating our PDMS molds. The photomasks have positive structures on them; in order to create sensors with same structures, we had to create a negative mold.

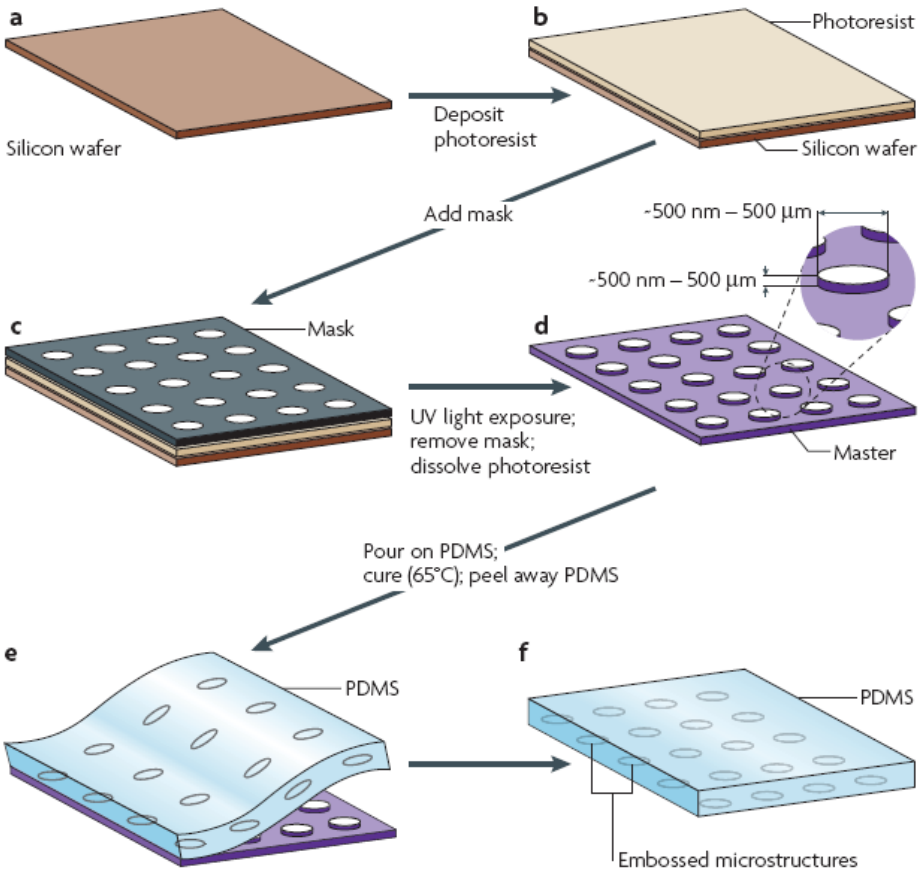


Figure 3-4: Soft-Lithography process ("Introduction about PDMS Soft-Lithography and Polymer Molding for Microfluidics").

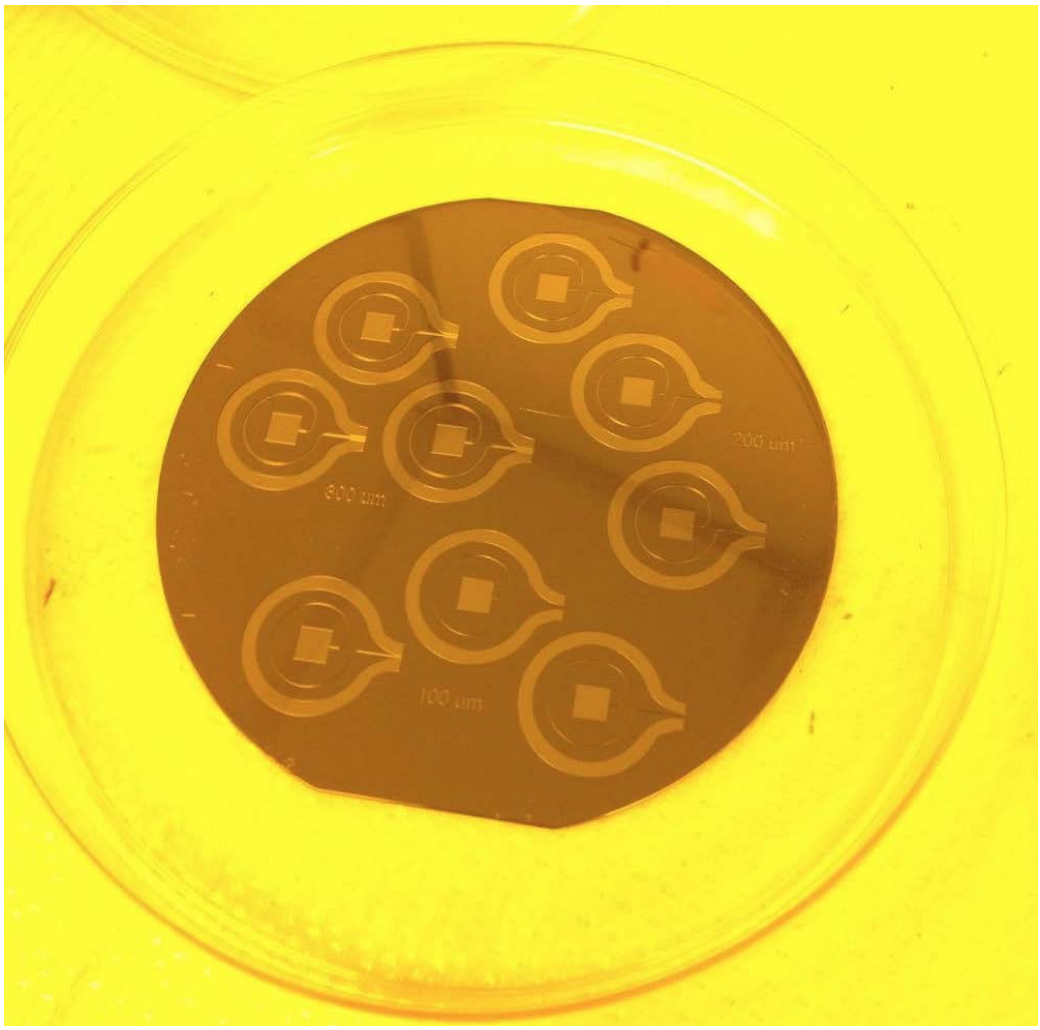


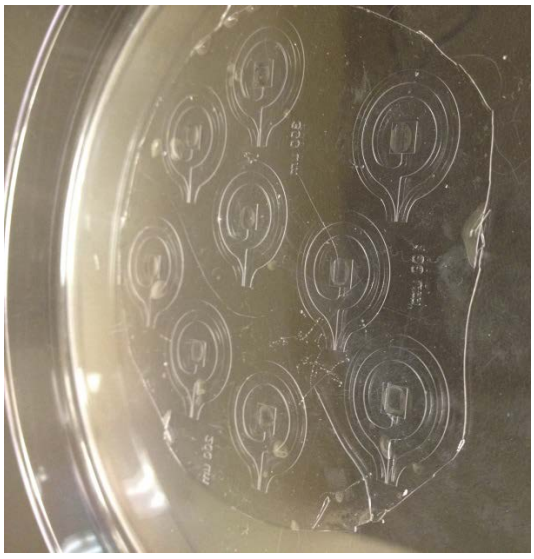
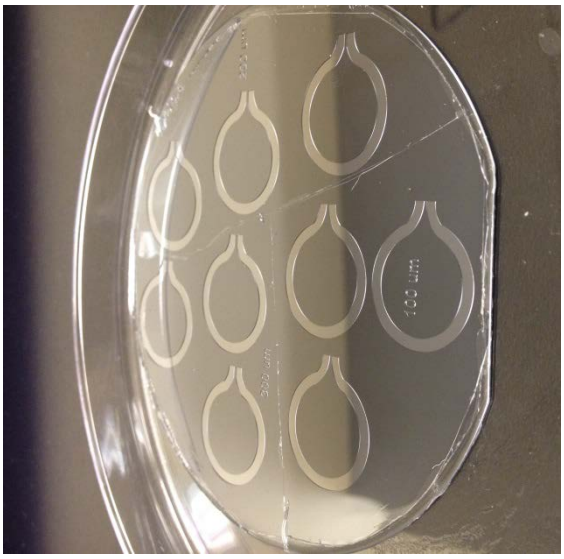
Figure 3-5: Completed photomask.

Once the photomasks were completed, we moved onto creating our PDMS molds. The photomasks have positive structures on them; in order to create sensors with same structures, we have to create a negative mold.

We treated the photomask with Trimethylchlorosilane (TMC5) for 20 minutes in a vacuum sealed chamber. (Explain what it does to the wafer). While the mask was being treated, we mixed a 10:1 mixture of PDMS and cross linker using a conditioning mixer in the lab. Our 10:1 PDMS mixture was mixed for two minutes and de-foamed for two minutes. Once the mask was treated, we spin coated it with a thin layer of PDMS for 45 seconds and cured it for at least one hour. After the PDMS was cured, we removed the PDMS layer from the mask, flipped them over so the negative structures would be facing up, and placed them in petri dishes for storage.

Initially, this was our main method of producing the PDMS molds; however, during our fabrication process much later into the year, we discovered that the gas chambers in our sensors were collapsing. To remedy this problem, we added one more step to this process. Instead of curing the PDMS coated mask for a full hour, we cured it for 40 minutes and repeated the same procedure for removing the PDMS from the mask. Once we got the PDMS layer into the petri dishes, we applied a single drop of PDMS to the negative structure that would become the gas chamber for the sensor. Applying this single drop of PDMS would increase the size of the chamber, thus preventing it to collapse onto itself.

Figure 3-6: Photomask spin coated with PDMS.

Figures 3-7 and 3-8: PDMS molds of top (3-7) and bottom (3-8) halves.

After creating our PDMS molds, we applied thin layers of epoxy to them to create the sensors using syringes to control the amount of epoxy we used. We then cured the sensors for 40 minutes under ultraviolet light. Initially, we used Epoxy 61 from the epoxy kit in the lab; however, we finally decided on using Epoxy 68 due to its flexible nature and high viscosity. We wanted to use a flexible, more viscous epoxy for our sensors because flexible materials can be read easier under ultrasound and the higher viscosity will slow down the receding of the epoxy from the tapered end of the mold while it is curing.

BONDING GUIDE

NOA Type	Viscosity	Refractive Index	Physical Characteristics	Adhesion to Glass	Adhesion to Metal	Adhesion to Plastic	Comments
60	300 cps	1.56	Tough	Good	Good	Fair	General purpose adhesive; has long shelf life.
61	300 cps	1.56	Tough	Excellent	Excellent	Fair	Preferred adhesive for precision optical bonding. Meets MIL-A-3920 Low shrinkage and resiliency of adhesive minimizes strain.
63	2000 cps	1.56	Hard, resilient	Good	Good	Fair	High viscosity adhesive useful for bonding u.v. opaque components by curing a bead or drop along edge. Cures well in thick sections.
65	1200 cps	1.52	Flexible	Good	Good	Fair	More flexible adhesive for extra low strain applications. Suitable for cold blocking applications.
68	5000 cps	1.54	Flexible	Excellent	Good	Good to Excellent	High viscosity adhesive designed for bonding plastics such as acrylic, polycarbonate and CAB.
81	300 cps	1.56	Hard, resilient	Excellent	Excellent	Fair	Extra fast curing adhesive for tacking, spot bonding or centering.

Figure 3-9: Bonding guide for the epoxy explaining different characteristics of the epoxy used.

Figure 3-10: Epoxy 61

Figure 3-11: Epoxy 68

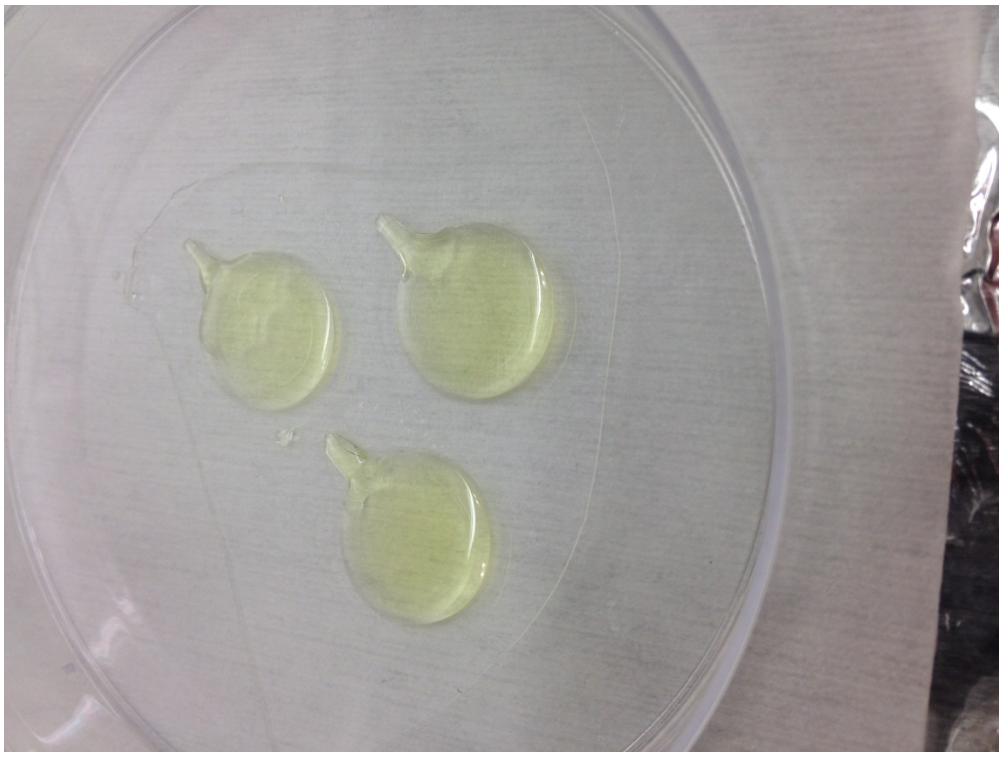


Figure 3-12: Cured Epoxy 61 on the PDMS molds.

Once the epoxy sensor halves have been cured, we prepared to attach them together. To do this we plasma treated the halves. This process includes exposing the surfaces of each half to plasma for one minute before lining up the channel and tapers and clamping them together. Once lined up and clamped they were further cured under ultraviolet light.

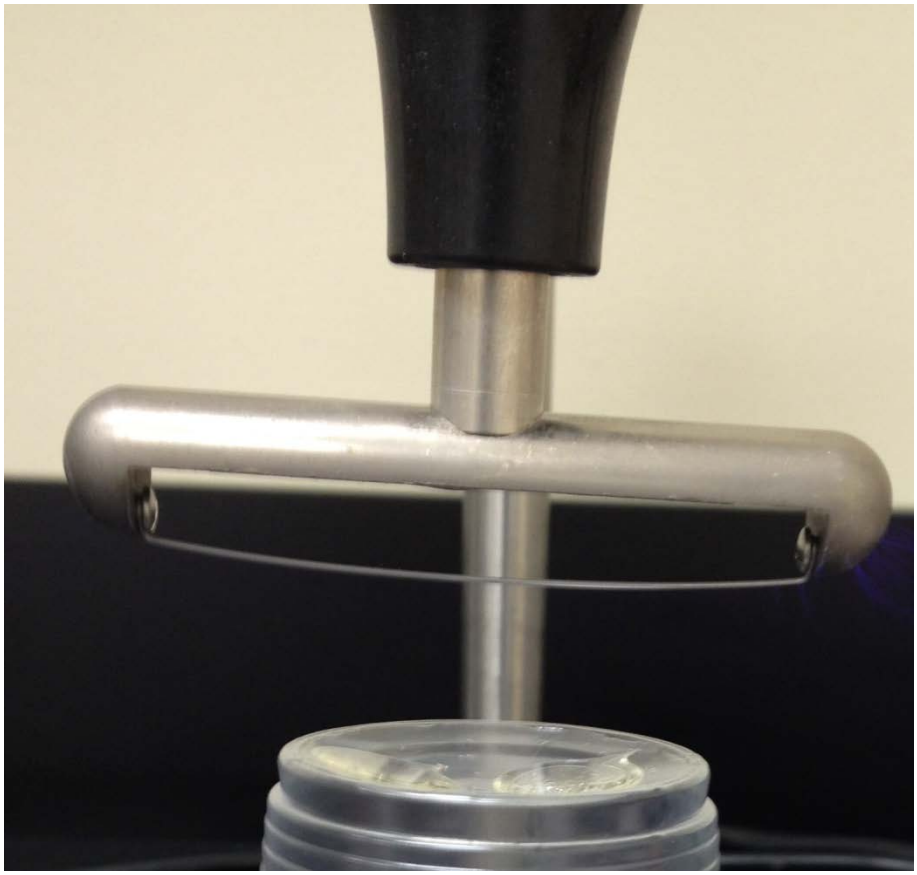


Figure 3-13: Plasma treatment of sensor halves. The plastic cup is used to place the sensor halves close to the device.

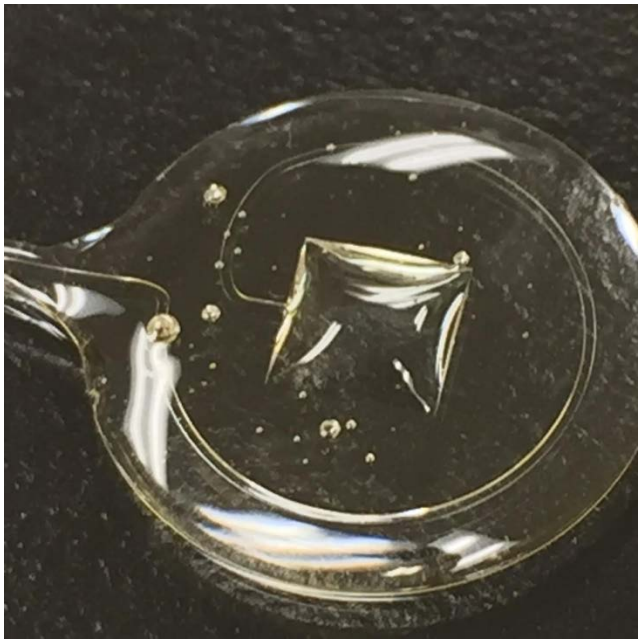


Figure 3-14: Sensor halves bonded together. This sensor is made from Epoxy 68.

With the sensor itself complete, the last step is fitting the capillary tube. We explored several different sizes and decided on 50 micron inner diameter round acrylic capillary tubing. This tubing was inserted into the 200 micron and 300 micron channels of the sensors and sealed into place with PDMS.

Figure 3-15: Completed prototype of 300 micron channel diameter Intracranial Pressure Sensor made with Epoxy 61 and 50 micron inner diameter capillary tube.

3.1.3 Testing

Normal ranges for intracranial pressure range from 50 to 15 mmHg. Pressures registering above 20 mmHg are abnormal and 40 mmHg begins to cause neurological issues such as dizziness, difficulty breathing, and compression of the brain. This sensor is able to accurately measure pressure ranges far above and below 0 mmHg and 60 mmHg. Our testing setup consisted of a chamber filled with water attached to a pressure simulating device called Elveflow. Elveflow is a flow control system that provides control of microfluidic pressure. We viewed the chamber under a light microscope which is connected to the software Infinity Analyze. Infinity Analyze allows for viewing and capturing of the microscopic images. We first tested our sensors without the capillary tubes attached and found that they were able to successfully register changes in pressure via a distance change in the gas/liquid interface. From here we attached the capillary tubes and proceeded to measure pressure using Elveflow to demonstrate pressure changes from 0 mBar to 30 mBar, or 0 mmHg to 22.5 mmHg, pressure changes that would begin to demonstrate unhealthy amounts of intracranial pressure. We tested up to 60 mBar to determine if the sensor would be able to successfully exceed the required pressure range.

3.2 Results

We were able to successfully test our sensor in water with and without the capillary tube attached. The sensor range easily captured the entire range of pressures we hoped to read and we were able to display a specific quantitative distance in the change in the gas/liquid interface for changes in pressure. The gas/liquid interface moved a distance of .912 millimeters for a pressure change of 30 mBar. This pressure change equates to 22.5 mmHg and demonstrates a range of pressure slightly above the normal, healthy range. The specific distance to pressure ratio is .152 millimeters for every 5 mBar, or 3.75 mmHg. Listed below are the results for the 200 micron diameter sensor.

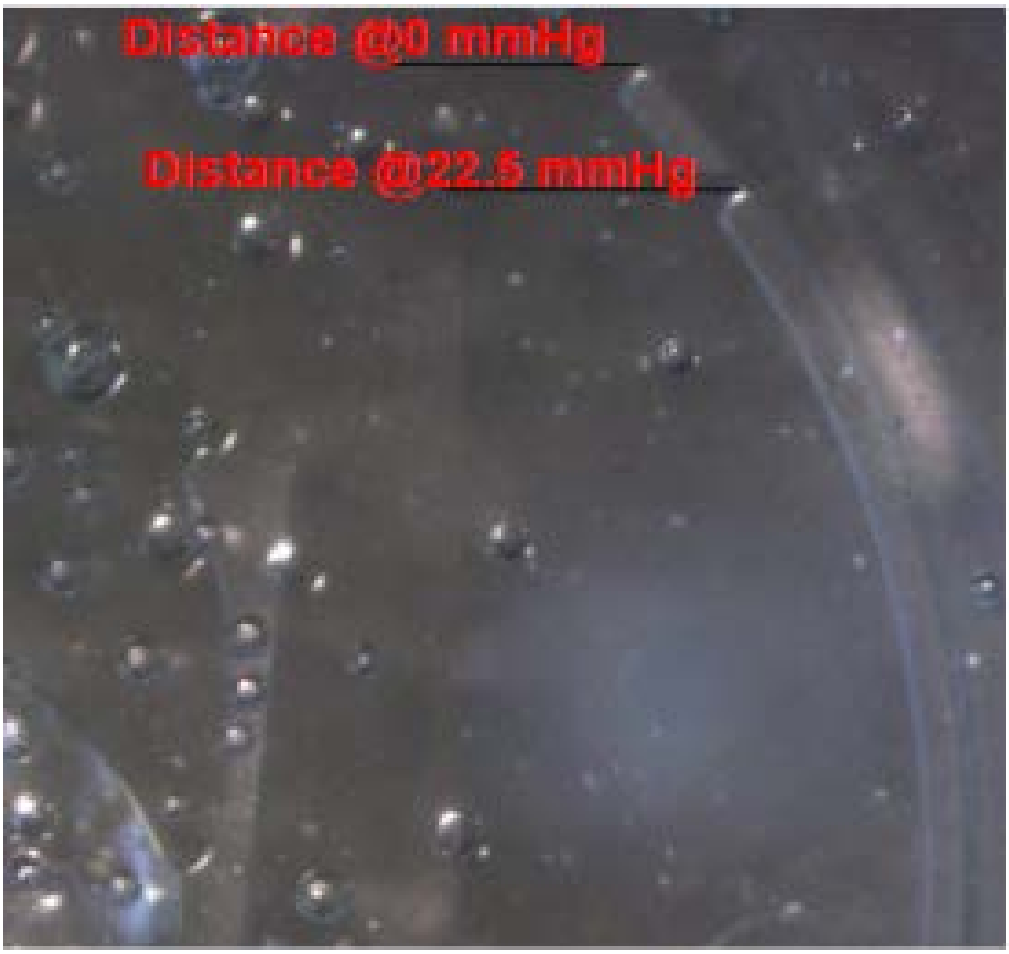


Figure 3-16: InfinityAnalyze images of pressure testing in water. The overlaid images show the change in position of the air-liquid interface from pressures 0mmHg to 22.5mmHg.

Distance(mm)	0	.152	.304	.456	.608	.76	.912
mBar	0	5	10	15	20	25	30
mmHg	0	3.75	7.5	11.25	15	18.75	22.5

Table 3-1: Results. Distance the gas-liquid interface travelled corresponding to changes in pressure.

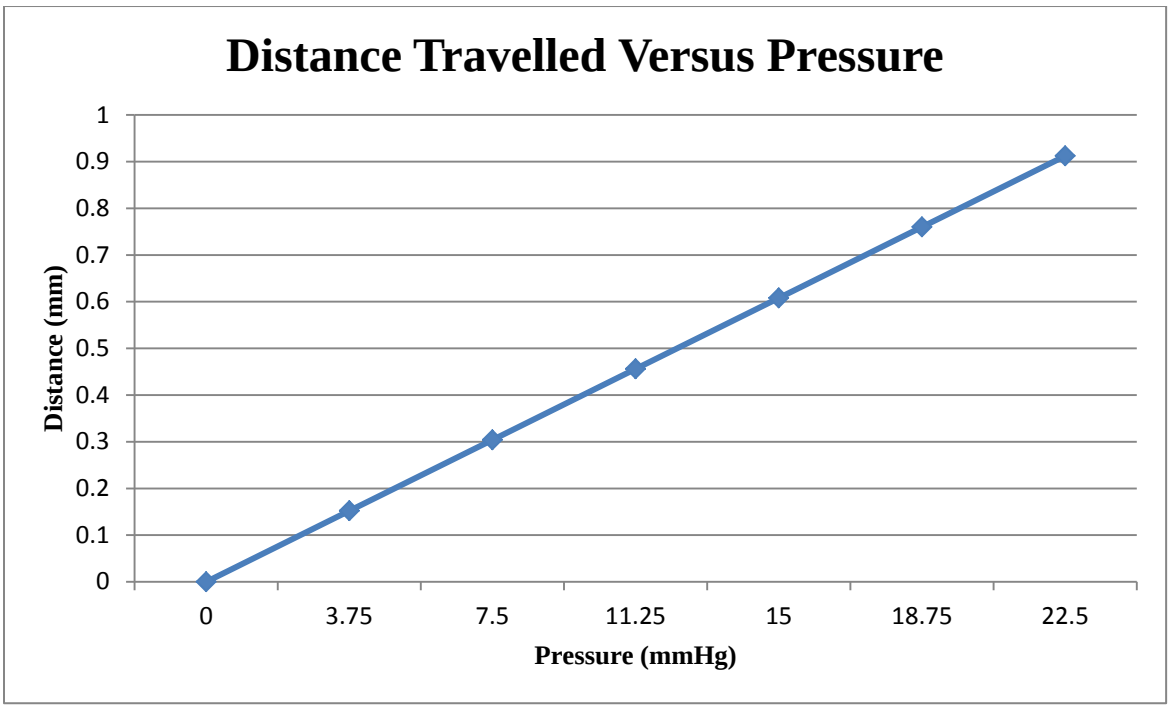


Figure 3-17: Graph of results. As the pressure increased, we saw a steady, linear increase in distance.

Chapter 4 - Cost Analysis

4.1 Overall Prototype Costs

Our initially proposed budget amounted to $1400. This consisted of approximately 5 3D Prints costing $500, ordering .5 Gallons of PDMS costing $300, $200 for various plastics and substrates, $300 for capillary tubes, with $100 dollars allotted for any miscellaneous items. We reassessed our budget and made a dramatic change to our initial method, switching from a 3D Print-based mold to a mold via Soft-Lithography. As our designs improved our prototype changed and the specific and overall costs decreased. Our final prototype consists of $200 for the analysis, completion and shipping of the masks for Soft-Lithography, $300 for .5 gallons of PDMS, $300 for various plastics and substrates, and $200 for Capillary tubes amounting to $1000.

4.2 Prototype Costs Versus Budget

Although our initially proposed budget entertained the cost of $1400, we received $1000 from our grant proposal and were required to reassess our costs. The first step was switching from a SolidWorks based design to AutoCAD. Not only did this decrease our overall cost by $300 dollars but it significantly increased our manufacturing output by allowing us to create several sensors from a single mask, as opposed to a single sensor from each 3D printed mold. Next we looked over our capillary tubes. Initially we were going to order six different capillary tube sizes: four sizes of round acrylic capillary tubing 1:2 ratio, one size of polycarbonate

capillary tubing 1:2 ratio and one size of polycarbonate capillary tubing 1:5 ratio. These rolls of capillary tubing cost 50 dollars each and after deliberation we decided to order two sizes of round acrylic capillary tubing 1:2 ratio, 50 microns and 100 microns, a 500 micron roll of polycarbonate capillary tubing 1:2 ratio and a 100 micron roll of polycarbonate tubing 1:5 ratio. Through analysis of our design process and manufacturing we were able to make changes to our proposed design to fit our budget.

Chapter 5 - Professional Issues and Constraints

5.1 Ethics

There are several ethical concerns regarding Intracranial Pressure Sensors. Intracranial Pressure Sensors are class three devices and require incredibly stringent testing prior to human trials. Most of this testing in regard to our sensors are mitigated due to the current research and procedures regarding Intracranial Pressure Sensors as well as shunts and their use in countering Idiopathic Intracranial Hypertension. It is no longer necessary to start from scratch in regard to physical interactions between the sensor and the brain as this device is an efficient combination of current methods that have already been approved and tested. It is important to also test toxicity, biocompatibility, stress-strain, and loading characteristics of the device. In the order of testing and implementing our device, we began testing in water for functionality, and would proceed to perform in vitro testing to determine the safety and efficacy of the sensor in a live environment.

5.2 Health and Safety

Biocompatibility testing and toxicity testing are both necessary. These tests ensure that the device will not have a negative reaction to the environment inside of the brain, either causing infection due to improper sterility, inciting an inappropriate

immune response, or poisoning the surrounding tissue. Testing for loading, as well as stress-strain testing, is also critical to ensure that the device will remain both fully functional and physical intact and pristine in the conditions inside the body and throughout the various pressure changes that are likely to exist. This will ensure that the device will not break due to the stress and strain placed on it inside the body as well as that the data the device provides and the device itself will maintain their integrity over time.

5.3 Manufacturability

The manufacturing process for our device consists of several steps allowing us to create nine sensors per mask. First PDMS is poured onto the mask, creating our mold. This is spin-coated on to create an even coat before it is incubated to solidify the mold. This process takes up to two hours, including the doctoring of the mold for the top half of the sensors to expand the volume of the reservoir. Next epoxy is poured into the PDMS mold to create the sensor halves. Pouring the epoxy takes time and precision as it is important to have an even, smooth distribution and to fill in every corner of the mold even with the epoxy receding against the PDMS. This is best accomplished through the use of an Ultraviolet gun, which allows for rapid curing of the epoxy before it can recede. With the epoxy cured, the next step is to plasma treat each sensor half and press them together, lining up the channels and tapers. The sensor should remain clamped together under ultraviolet light for approximately an hour. After the sensor is plasma bonded the capillary tube needs to be attached. There is no overly efficient method for inserting the capillary tube currently and it requires slow precision and hand-eye coordination to line up the 100 micron outer diameter capillary tube with the 200 micron channel opening. Once this has been accomplished, PDMS is inserted into the taper and cured to hold the capillary tube in place. Currently it takes one and a half days to complete a batch of sensors with nine sensors completed with each batch. The process can be streamlined

through the use of an UV gun as well as utilizing multiple masks to create more sensors at a time.

5.4 Usability

The intracranial pressure sensor will be used as a method to treat and diagnose idiopathic intracranial hypertension. It will be inserted via surgery near the hairline on the skull. A hole will be drilled through the skull to insert the capillary tube into the brain cavity while the sensor will be placed outside the skull to provide access via ultrasound. When inserted, fluid enters the capillary tube going up into the sensor until it reaches a point of equilibrium with the gas inside the gas reservoir. This gas/fluid interface will be used to define the current point of pressure of the cerebral fluid. This sensor will be read through the use of an ultrasound machine, and the pressure will be determined based on the location of the gas/fluid interface. This device will provide a readout of the pressure of the cerebral fluid. This can be used to determine the condition and status of the idiopathic intracranial hypertension and immediately determine if additional catheters are needed to drain the cerebral fluid. The intracranial pressure sensor works in conjunction with catheters to diagnose and alleviate symptoms caused by idiopathic intracranial hypertension.

5.5 Sustainability

Our sensor, once implanted, is intended to remain inside the patient's head. Due to this, it is a long lasting, yet single use product. Waste does not accrue through the use of this product. If we look at the production of the Intracranial Pressure Sensor, the manufacturing process is relatively sustainable. The production of the molds uses

PDMS, a silicone based material. If stored and treated properly the PDMS molds can be used several times before needing to be spin-coated again. This severely diminishes the amount of PDMS needed to create the sensors. In regard to the excess PDMS generated, PDMS is a non-volatile substance. In addition, when it comes into contact with soil, it has been found to degrade into lower molecular weight compounds. PDMS is not hazardous to the environment, and even in the event of mixing with water, it attaches to particulates and is filtered from the water through sedimentation. Overall our manufacturing process is clean, efficient, and sustainable.

Chapter 6 - Conclusion

6.1 Summary

Idiopathic Intracranial Hypertension is a condition that occurs when the pressure within the cranial cavity increases for an undetermined reason. This condition can cause significant permanent damage to the brain and eyes if left untreated. The Intracranial Pressure Sensor is designed to aid in the diagnosis and treatment of Idiopathic Intracranial Hypertension by draining the cerebrospinal fluid in the skull while providing immediate readouts of the pressure within the skull. Previously patients would have to wait until symptoms reappeared to determine if their catheters were clogged, requiring further surgery. The Intracranial Pressure Sensor can seriously mitigate and reduce the damage done by Idiopathic Intracranial Hypertension by allowing immediate knowledge of increased pressure within the skull. The manufacturing process begins with masks created via Soft-Lithography. From these masks we create PDMS molds to which we fill with epoxy and cure to generate our sensor halves. The sensor halves are plasma bonded together and then a capillary tube is inserted into the channel. PDMS is used to bond the capillary tube in place. The sensor can successfully register changes in pressure from 0 mmHg to greater than 50 mmHg with notable, measurable physical changes within the gas/liquid interphase in the sensor.

6.2 Future Plans

The primary plan is to test the intracranial pressure sensor under an Ultrasound machine. Once we have tested the visibility we can begin addressing the specificity of the pressure readout. Currently the pressure sensor demonstrates a 0.3 millimeter

change for a 7.5 mmHg increase or decrease in pressure. While this does enable a completely visible change under a light microscope, to generate greater accuracy in reading we will increase the distance the gas/liquid interface moves to create a more obvious readout for small pressure changes. This can be accomplished by increasing the size of the gas/liquid reservoir while minimizing the size of the channels within the pressure sensor.

6.3 Lessons Learned

The creation of the intracranial pressure sensor exposed us to a diverse range of skills and techniques. We effectively demonstrated good laboratory practices which were necessary for the completion of each step in manufacturing our device. We learned how to further use SolidWorks and AutoCAD to create digital models of our device. We worked with Soft-Lithography, and learned how to prepare and use PDMS in the creation of our molds. Through the creation of the sensors itself we worked with epoxy, learning about different material characteristics as well as the mechanics of plasma bonding through which we connected our sensor halves. We learned how to address a design process, to set deadlines and work through a series of connected steps necessary to complete the manufacturing of our sensors while maintaining a budget. We learned how to accurately quantify data and how to work through difficulties and setbacks with materials and lab equipment. Through our design process we learned and demonstrated collaboration, working together in both design and the manufacturing of our sensor.

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Appendix A: Grant Proposal

Intracranial Pressure Sensor

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There are several diseases that cause increased pressure in the brain. This can lead to increased blood pressure, headaches, nausea, and decreased mental abilities. Shunting is the practice used to treat increased intracranial pressure by redirecting excess cerebrospinal fluid from the brain cavity into another body cavity through the use of two catheters. These catheters have the tendency to become clogged, and the intracranial pressure will begin to increase again. Without an intracranial pressure sensor, the only way to detect the failure of the catheters would be through waiting for appropriate symptoms to begin to show, which may take weeks to months and cause serious damage. We propose to create an Intracranial pressure sensor which can be read through either infrared or Ultrasound to determine the current pressure in the cranial cavity. This would provide immediate knowledge of clogged catheters, preventing further damage to accrue due to an unknown buildup of pressure, prior to, and when symptoms begin to show. This would greatly improve the quality of life of the individuals who are suffering from Idiopathic Intracranial Hypertension and other similar diseases that cause the buildup of fluid in the brain cavity by allowing the efficacy of their shunts to be easily monitored and regulated before they begin to suffer from the symptoms that typically occur when left untreated.

We are partnering with Sean Murray Medical Corporation to obtain access to an Ultrasound Machine. They will aid in the development and testing of this product as well as providing trained technicians who are able to determine and read the Ultrasound results.

Materials	Cost
3D Printing x5	$500
.5 Gallons of PDMS	$300
Various Plastics and Substrates	$200
Chemicals for bonding	$300
Miscellaneous	$100
~	~
Total Cost	$1400

We recognize that acceptance of any from the Dean's Office commits us to presenting our project in a poster session at Family Weekend in February, Preview Weekend in April and the Spring Engineering Education Days (SEEDs) program, also in April.

10/23/2015

I, J. Enrearaci, have reviewed and support this team's proposal for Engineering Undergraduate Programs Senior Design Funding.

10/23/2015

Appendix B: List of Abbreviations

CSF-Cerebrospinal Fluid

GAT-Goldmann Applanation Tonometry

ICPS-Intracranial Pressure Sensor

IIH-Idiopathic Intracranial Hypertension

IOP-Intraocular Pressure

PDMS-Polydimethylsiloxane

TMC5-Trimethylchlorosilane

UV-Ultraviolet